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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,884	10/23/2000	Kiyozo Asada	1422-443P	6983

2292 7590 08/25/2004

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EXAMINER	
SPIEGLER, ALEXANDER H	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,884	ASADA ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,16-18,21-23 and 31-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,16-18,21-23 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2004 has been entered.

Status of the Application

2. Claims 1, 5-9, 16-18, 21-23, 31-35 are pending and rejected herein. This action is made NON-FINAL. Any objections and rejections not reiterated below are hereby withdrawn. Specifically, the claim objection to Claim 35 and the 112, 1st paragraph rejection has been withdrawn in view of Applicants amendments. It is noted that Applicants list Claim 35 as withdrawn, however, in view of Applicants amendment to Claim 35, Claim 35 is now pending, and not withdrawn. Furthermore, the 102 and 103 rejections in view of Chetverin have been withdrawn in view of Applicants' amendment of "water-soluble" and Applicants argument that Chetverin teaches a solid media and not "water-soluble" acidic macromolecular substances encompassed by the claims. In addition the 103 rejection of Sorge in view of Gaugler has been withdrawn in favor of the 102 rejection over Sorge. The 102 rejections of Blakely, Koster, Sorge and Barton have been maintained. New rejections are also contained herein.

Claim Interpretation

3. The term "DNA synthesis reaction-enhancer" has been interpreted as comprising any cationic complex or water-soluble acidic macromolecular substance encompassed in Claim 1. Accordingly, if the prior art teaches the identical chemical structure of the compounds encompassed in Claim 1, the properties applicant discloses and/or claims are necessarily present. See MPEP § 2112.01.

The specification defines "DNA synthesis reaction-enhancer" as, "the acidic substance or cationic complex mentioned above alone, or a mixture comprising both the acidic substance and cationic complex, each of which is capable of exhibiting an action of enhancing DNA synthesis reaction." (See page 5, lines 22-25). Accordingly, because the cationic complexes or water-soluble acidic macromolecular substances encompassed in Claim 1 are "capable of exhibiting an action of enhancing DNA synthesis reaction," prior art that teaches the products of Claim 1 has been interpreted as anticipating the claimed invention (at least with respect to Claim 1).

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Blakely et al. (USPN 5,418,162)

Regarding Claims 1 and 16, Blakely teaches heparin sulfate, which is a "DNA synthesis reaction-enhancer." (See col. 16, line 26). Furthermore, Blakely teaches performing PCR with a primer (e.g., DNA which does not serve as the template for DNA synthesis). (See col. 16, lines 1-12).

Regarding Claim 17, Blakely teaches the synthesis reaction composition comprising DNA polymerase.

Applicants Arguments

Applicants argue Blakely teaches that heparin sulfate prevents non-specific adsorption of nucleic acid probes to filters, and therefore does not teach the enhancement of a DNA synthesis reaction by heparin sulfate during DNA synthesis. (See Applicants arguments on page 10)

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, Applicants' are arguing limitations that are not required by the claims. Claim 1 is drawn to a product, "a DNA synthesis reaction enhancer," comprising heparin sulfate or DNA that does not serve as a template for DNA synthesis, and not a method of enhancing DNA synthesis or a method of using a product. Therefore, since Blakely teaches the product of heparin sulfate and DNA which does not serve as a template for DNA synthesis (e.g., a primer), Blakely anticipates the claimed invention. See discussion under section titled, "Claim Interpretation" above in ¶ 3.

6. Claims 1, 16-18, 21-23 and 31-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Koster et al. (USPN 5,928,906).

Regarding Claims 1 and 16, Koster teaches DNA that does not serve as a template (e.g., a primer) and a cationic complex (Mg 2+) for use in enhancing DNA synthesis reactions. (See col. 12, for example)

Regarding Claims 17-18 and 21, Koster teaches the composition comprising one DNA polymerase having 3'→5' exonuclease activity (e.g., *Pyrococcus furiosus*), and another DNA polymerase having no 3'→5' exonuclease activity (e.g., Taq polymerase). (See cols. 7-8, for example)

Regarding Claims 22 and 35, Koster teaches the composition comprising two or more kinds of DNA polymerase having 3'→5' exonuclease activity that is not reduced. (See cols. 3, 7-8, for example)

Regarding Claim 23, Koster teaches the composition comprising a α-type DNA polymerase and a non α-type DNA polymerase. (See cols. 7-8)

Regarding Claims 31-34, Koster teaches kits comprising a DNA synthesis reaction enhancer, two or more kinds of DNA polymerases, and reagents usable for DNA synthesis. (See col. 3, lines 34-45, and cols. 7-8, for example).

7. Claims 1, 16-18, 21-23 and 31-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Sorge et al. (USPN 5,556,772).

Regarding Claims 1 and 16, Sorge teaches DNA that does not serve as a template (e.g., a primer) and a cationic complex (Mg 2+) for use in enhancing DNA synthesis reactions. (See cols. 6-9, for example)

Regarding Claims 17-18 and 21, Sorge teaches the composition comprising one DNA polymerase having 3'→5' exonuclease activity (e.g., *Pyrococcus furiosus*), and another DNA polymerase having no 3'→5' exonuclease activity (e.g., Taq polymerase). (See abstract and cols. 2-4, for example)

Regarding Claims 22 and 35, Sorge teaches the composition comprising two or more kinds of DNA polymerase having 3'→5' exonuclease activity that is not reduced. (See abstract and cols. 2-4, for example)

Regarding Claim 23, Sorge teaches the composition comprising a α-type DNA polymerase and a non α-type DNA polymerase. (See cols. 2-4, for example)

Regarding Claims 31-34, Sorge teaches kits comprising a DNA synthesis reaction enhancer, two or more kinds of DNA polymerases, and reagents usable for DNA synthesis (including DNA that does not serve as a template). (See col. 2, lines 45-54, and col. 5, lines 7-19, for example).

Applicants Arguments with Respect to 102 Rejections over Koster and Sorge

> Applicants' argue:
>
> Koster '906 and Sorge '772 disclose nucleic acid amplification carried out in the presence of Mg 2+ and two polymerases. However, while Mg 2+ is a cofactor essential for strand extension by DNA polymerase, the Mg 2+ is not a complex ion as used in the present invention, or a complex ion is not formed therewith. Therefore, neither Koster '906 nor Sorge '772 disclose or suggest the enhancement of a DNA synthesis reaction by Mg 2+ during DNA synthesis.

(See Applicants' arguments on page 11)

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, the specification does not specifically define "cationic

complex," and therefore, Mg 2+ and its use in an amplification buffer is considered to encompass a "cationic complex." Furthermore, since the claims encompass "DNAs which do not serve as templates for subject DNA synthesis," and Koster and Sorge each teach the use of DNA primers (which do not serve as templates for subject DNA synthesis), Koster and Sorge anticipate the claimed invention.

8. Claims 1, 6-8 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Barton (USPN 5,225,556).

Regarding Claims 1, 6-8 and 16, Barton teaches a DNA synthesis reaction enhancer comprising a cationic complex wherein said cationic complex is a transition element of the Group VIII (Co). (See abstract and cols. 10-16)

Applicants Arguments

Applicants argue:

> The present invention is distinguishable from Barton in that a cationic complex exhibiting the ability to enhance a DNA synthesis reaction is used as described on page 10, lines 4-22 of the specification. Specifically, the transition metal complex may be any complex capable of exhibiting an action of enhancing DNA synthesis. For this reason, Barton '556 fails to anticipate the present invention.

(See Applicants response on page 11)

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, Applicants' are arguing limitations that are not required by the claims. Claim 1 is drawn to a product, "a DNA synthesis reaction enhancer," comprising a cationic complex wherein said cationic complex is a transition element of the Group VIII (Co), and not a method of enhancing DNA synthesis or a method of using a product. Therefore, since Barton teaches the product of a cationic complex wherein said cationic

complex is a transition element of the Group VIII (Co), Barton anticipates the claimed invention. See discussion under section titled, "Claim Interpretation" above in ¶ 3.

NEW REJECTIONS

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 5-9, 16-18, 21 and 31-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims have been amended to recite, "[a] DNA synthesis reaction-enhancer comprising at least one kind selected from group consisting of cationic complexes and *water-soluble* acidic macromolecular substances, wherein said *water-soluble* acidic macromolecular substances are one or more substances selected from the group consisting of sulfated-fucose-containing polysaccharides, dextran sulfate, carrageenan…". (emphasis added)

Applicants assert there is support for the recitation of "water-soluble" on page 8, lines 14-19, which states, "[t]he *salts* of the acidic substances described above are not particularly limited, as long as they have an action of enhancing DNA synthesis reaction,

with preference given to *water-soluble salts*. For example, there are included alkali metal salts such as sodium dextran sulfate, sodium alginate...". While there is support for water-soluble *salts* of the acidic macromolecular substances listed on page 8, there is not support of the recitation of "water-soluble acidic macromolecular substances...selected from the group consisting of sulfated-fucose-containing polysaccharides, dextran sulfate, carrageenan...". Accordingly, because Claim 1 encompasses water-soluble acidic macromolecular substances other than water-soluble *salts* of acidic macromolecular substances, the amended claims recite new matter.

Furthermore, if "salts thereof" refers to salts of cationic complexes or salts of DNAs which do not serve as templates for subject DNA synthesis, it is not clear where there is support for this recitation. Applicants are requested to clarify where there is support for this recitation.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 5-9, 16-18, 21-22 and 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 5-9, 16-18, 21 and 31-35 are indefinite over "salts thereof" because it is not clear as to whether this refers to salts of all of the cationic complexes and water-soluble acidic macromolecular substances encompassed by the claims, or some of the acidic macromolecular substances, or salts thereof "DNA which do not serve as templates for subject DNA synthesis," etc. If "salts thereof" refers to salts of all of the cationic complexes and water-soluble acidic macromolecular substances encompassed by the

claims, then it is not clear as to what encompasses salts thereof "cationic complexes" and "DNA which do not serve as templates for subject DNA synthesis." Furthermore, Claims 1, 5-9, 16-18, 21 and 31-35 are indefinite over "subject DNA synthesis" because it is not clear as to what is meant by or encompassed by "subject DNA synthesis." The specification does not define this recitation.

B) Claim 21 is indefinite over "the other polymerase" because this recitation lacks antecedent basis, since Claim 18, from which Claim 21 depends from, refers to "two or more kinds of DNA polymerases," but does not refer to "the other DNA polymerase."

C) Claim 22 is indefinite over "not reduced" because it is unclear as to what is encompassed by this phrase and it is not clear as to what is being compared to conclude that the activity is not reduced. (e.g., a wild type/unmodified DNA polymerase, a different DNA polymerase, etc.)

Claim Rejections - 35 USC § 102

13. Claims 1 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by the Sigma Catalog (1996).

Regarding Claims 1 and 16, Sigma teaches the DNA synthesis reaction enhancer comprising, dextran sulfate (pages 337-338), heparin (pages 531-532), dermatan sulfate (chondroitin sulfate B) (page 268), heparan sulfate (page 531), hyaluronic acid (pages 549-550), alginic acid (page 76), pectin (page 786), polyglutamic acids (page 1959), and polyvinyl sulfates (page 864).

14. Claims 1, 5 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Sakai et al. (USPN 6,207,652).

Regarding Claims 1, 5 and 16, Sakai teaches the DNA synthesis reaction enhancer comprising sulfated-fucose-containing polysaccharide-F and sulfated-fucose-containing polysaccharide-U. (See cols. 1-2)

15. Claims 1, 6-9 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Tavitigian et al. (USPN 5,789,206).

Regarding Claims 1, 6-8 and 16, Tavitigian teaches a DNA synthesis reaction enhancer comprising a cationic complex wherein said cationic complex is a transition element of the Group VIII (Co). (See col. 6, lines 65-66)

Regarding Claim 9, Tavitigian teaches a DNA synthesis reaction enhancer comprising hexamine cobalt (III) chloride. (See col. 6, lines 65-66)

Conclusion

16. No Claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (571) 272-0747. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Alexander H. Spiegler
August 11, 2004

CARLA J. MYERS
PRIMARY EXAMINER